

GUEST EDITORIAL

Twenty twenty ... two: Headache and COVID-19

"Twenty twenty ... two" was how some people sarcastically welcomed the year 2022 on New Year's Eve. But there is more than sarcasm behind the statement: probably a superstitious ritual to avert having the 2020 scenario strike again. The coronavirus disease 2019 (COVID-19) pandemic outbreak in 2020 will be always etched in our memory: the deaths, the suffering of the patients and their families, the lockdown, and the efforts of health-care professionals and scientists to fight severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Two years later, the world is still facing SARS-CoV-2. For instance, a remarkable increase in COVID-19 cases have been registered in January 2022 in several countries and cities like Shanghai are again under lockdown as this editorial is being written.

Hence, despite the time passed, SARS-CoV-2 and COVID-19 are still among us and certainly a hot topic.

Yet, the setting has changed compared to 2020. New SARS-CoV-2 variants have emerged; for example, Omicron is responsible for the latest wave, and treatments for COVID-19 as well as preventive strategies that include vaccinations are available. All these factors had and still have an important impact in determining the evolution of the pandemic over these 2 years.

As the pandemic has continued, we have also started to realize the central role that headache has in SARS-CoV-2 infection.

Headache has gone from being considered a second-tier symptom of COVID-19 to one of the most relevant manifestations. This conceptual change has been driven by the clear prominence of headache as a COVID-19 symptom, and the unprecedented number of studies that analyzed headache in the setting of the SARS-CoV-2 infection.¹⁻⁵ In the review "Headache associated with COVID-19: epidemiology, characteristics, pathophysiology and management," the authors give a useful overview of the published literature.⁶ We now know that headache is common, disabling, and represents frequently a difficult-to-treat persistent symptom.

In support of these findings, in the last 2 years, it has not been infrequent to observe that, in clinical practice, people with a new-onset headache, even as a unique symptom, or worsening of a usual one, are immediately tested to rule out SARS-CoV-2 infection. This is a clear sign of how relevant the general population and health-care professionals now perceive headache to be, and how this symptom has been so strongly associated with COVID-19.

But, several other points are worth emphasizing after reading this review. First, study cohorts of published works mainly belong to the first wave of the pandemic, a fact that raises the question of the impact that the new variants and the available treatments, as mentioned earlier, may have not only on the pandemic but also on

headache. Second, controversies exist, especially in terms of epidemiology of who develops headache with SARS-CoV-2 infection and the underlying pathophysiology of that headache. The different methodology used in the published studies makes comparisons difficult, underscoring the need for new and more standardized studies to clarify the true prevalence, the risk factors of headache attributed to SARS-CoV-2, and its putative pathophysiological mechanisms, specifically those involving inflammation. Third, there are no available standard-of-care treatments for headache attributed to COVID-19, making the management of patients extremely variable and probably suboptimal, especially for those with persistent headaches, who may be commonly seen in clinical practice. This increases the burden of headache in individuals and, at a higher level, in society.

The truth is that headache attributed to systemic viral infection and other secondary headaches that are on its differential diagnosis have never received this much attention in the past as they have now since the beginning of the pandemic.⁷ Yet, we are still missing a lot of data, to better understand and treat headache in the setting of COVID-19.

As SARS-CoV-2 and its sequelae will probably live with us for a long time, we still need more scientific efforts to fight COVID-19. So, "twenty twenty ... two" should represent a positive motto, indicating the need to renew in the scientific community the motivation observed in early 2020 to continue investigating COVID-19, and specifically headache.

This is the only way to answer all these open questions and keep doing the best for our patients.


KEYWORDS

COVID-19, epidemiology, headache

CONFLICTS OF INTEREST

Dr. Caronna has received honoraria from Novartis and Chiesi. Dr. Pozo-Rosich has received honoraria as a consultant and speaker for: Allergan-AbbVie, Almirall, Biohaven, Chiesi, Eli Lilly, Medscape, Neurodiem, Novartis, and Teva. Her research group has received research grants from Novartis; has received funding for clinical trials from Alder, Amgen, Electrocore, Eli Lilly, Novartis, and Teva. She is a trustee member of the board of the International Headache Society and the Council of the European Headache Federation. She is on the editorial board of *Revista de Neurologia*. She is an editor for *Cephalalgia*, *Headache*, *Neurologia*, *Frontiers of Neurology*, and advisor for *The Journal of Headache and Pain*. She is a member of the Clinical Trials Guidelines Committee of the International Headache

Society. She has edited the *Guidelines for the Diagnosis and Treatment of Headache* of the Spanish Neurological Society. She is the founder of www.midolordecabeza.org. She does not own stocks from any pharmaceutical company.

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